REMARKS

Claims 5, 8, 9, 18, 21, 22, 31, 34, 35, 44, 47, 48, 53-56, 58-81 and 83-89 have been withdrawn from consideration. Claims 1-4, 6, 7, 10-17, 19, 20, 23-30, 32, 33, 36-43, 45, 46, 49-52, 57, and 82 are currently under examination. Claims 1, 2, 7, 14, 15, 20, 27, 28, 33, 40, 41, 46, 57, and 82 are currently amended. The amendments are supported by the original claim language and the specification as originally filed. No new matter is introduced by this Response, and thus entry thereof is respectfully requested.

I. AMENDMENTS TO THE ELECTED INVENTION

Applicants acknowledge, with appreciation, the Examiner's indication that the response filed April 9, 2009 was a *bona fide* attempt to reply to the Office Action of October 10, 2008. The claims as currently presented have been amended to reflect the elected invention of detecting the expression level of ABCC5, GTF2H2 and ERCC2.

In view of the foregoing, Applicants respectfully request objections to the pending claims be withdrawn.

Reconsideration of the application in view of the current claims is respectfully requested and further in view of the following remarks in response to the claim rejections asserted by the Examiner in the Office Action of October 10, 2008.

II. CLAIM REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner has rejected claims 1-4, 6, 7, 10-13, 20, 33, 40-43, 45, 46, 49-52, 57 and 82 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner asserts that claims 1-4, 6, 7, 10-13, 40-43, 45, 46, 49-52 and 82 are indefinite over the recitation of "certain level." Claims 2-4, 6, 7, 10-13 are dependent on claim 1 and includes all of the limitations of claim 1. Claims 53-43, 45, 46, 49-52 are dependent on claim 40, and include all of the limitations of claim 40. Applicants respectfully traverse the above rejection as current claims 1, 40, and 82 identify the agent based on an expression level that is comparable to a previously determined level of at least one of the marker genes, or a

previously determined level of two or more of the marker genes, in cells with known sensitivity to an agent, and is supported by the specification (see for example paragraphs [0011], [0188]).

The Examiner asserts claims 1-4, 6, 7, and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. Claims 2-4, 6, 7, 10-13 are dependent on claim 1 and includes all of the limitations of claim 1. Applicants respectfully traverse the above rejection because claim 1 is not omitting a step. Claim 1 claims a method for determining whether an agent can be used based on the expression of a marker gene and does not require treating the cells with the agent. Furthermore, the current claim includes identifying the agent based on an expression level that is comparable to a previously determined level of the marker gene in cells with known sensitivity to an agent, thus identifying a relationship between the agent and the expression level of the marker.

The Examiner asserts claim 2 is indefinite over the recitation of "said tow [two] or more ma[r]kers" because this phrase lacks proper antecedent basis. Applicants respectfully traverse the above rejection as current claim 2 no longer includes the aforementioned recitation.

The Examiner asserts claims 7, 20, 33, and 46 are indefinite over the recitation of "expanded group of genes represented by genes" and of "positively or negatively associated." Applicants respectfully traverse the above rejection as current claims 7, 20, 33, and 46 no longer include the aforementioned recitations.

The Examiner asserts claims 7, 20, 33 and 46 are indefinite over the recitation of IGEI. Applicants respectfully traverse the above rejection as current claims 7, 20, 33, and 46 include "wherein said IGEI comprises a ratio of the level of expression of at least two marker genes."

The Examiner asserts claim 20 as indefinite over the recitation of the negatively associated genes. Applicants respectfully traverse the above rejection as current claim 20 no longer includes the aforementioned recitation.

The Examiner asserts claim 57 as indefinite because the claim does not recite a clear nexus between the preamble of the claim and the final step of the claim. Applicants respectfully traverse the above rejection as current claim 57 includes step (e), providing how comparing a

first and second IGEI results in the determination that an agent modulates the onset or progression of cancer.

Based on the reasons provided above, withdrawal of the rejections under 35 U.S.C. 112, second paragraph, is respectfully requested.

III. CLAIM REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

The Examiner has rejected claims 1-4, 6, 7, 10-17, 19, 20, 23-30, 32, 33, 36-43, 45, 46, 49-52, 57 and 82 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner asserts that claims 1-4, 6, 7, 10-13 and 82 and claims 40-43, 45, 46, and 49-52 are drawn to a methods comprising identifying an agent based on at least one of the marker genes is expressed at "a certain level" and the claims and specification do not define the "certain level" of expression. Applicants respectfully traverse the above rejections. Claims 2-4, 6, 7, 10-13 are dependent on claim 1 and includes all of the limitations of claim 1. Claims 41-43, 45, 46, and 49-52 are dependent on claim 40 and includes all the limitations of claim 40. As discussed above, current claims 1, 40, and 82 identify the agent based on an expression level that is comparable to a previously determined level of at least one, or comparable to a previously determined level of two or more, of the marker genes in cells with known sensitivity to an agent, and is supported by the specification (see for example paragraphs [0011], [0188]) and thus sufficiently enables a person of ordinary skill in the art to perform methods claimed.

The Examiner asserts with the exception of claim 57, the claims encompass methods in which any type of cancer cell is analyzed to identify an agent for treating cancer. Current claims 1, 14, 27, 40 and 82 claim methods for analyzing lung cancer cells. As such, the pending claims encompass methods for lung cancer cells.

The Examiner asserts claim 3 requires that ABCC5, GTF2H2 and ERCC2 are miRNAs and claims 16, 29, and 42 require that ABCC5, GTF2H2 and ERCC2 are siRNAs. Current claims 3, 16, 29, and 42 claim that the transcribed polynucleotide is an mRNA.

The Examiner asserts the present claims appear to require a known relationship between the expression levels of ABCC5, GTF2H2 and ERCC2 and the occurrence of cancer. The

Examiner further asserts the findings of the specification "does not allow one to generate a method for identifying new agents that are effective for treating cancer" because the teaching of an association between marker levels lung cancer cell lines and drug resistance is not equivalent to a teaching that the markers are correlated with the occurrence of cancer.

Applicants respectfully disagree. The instantly claimed methods are for identifying agents that are effective in treating lung cancer cells and would not require the marker levels to be related or correlated to the occurrence of cancer. The marker levels are indicative of sensitivity to an agent. As the Examiner notes, the specification has provided information regarding the level of expression of ABCC5, GTF2H2 and ERCC2 in lung cancer cells and their correlation with an agent for treating cancer. Thus, the specification provides guidance and direction for the instantly claimed methods of analyzing lung cancer cells and their responsiveness to agents for treating lung cancer, which includes predicting and monitoring a patient's response to treatment with an agent for lung cancer.

The Examiner also asserts that the specification does not teach or provide sufficient guidance in determining a particular level of gene expression of ABCC5, GTF2H2 and ERCC2 for the instantly claimed methods. Furthermore, the Examiner states the specification does not provide sufficient guidance as to additional interactive indices of expression without undue experimentation. Applicants respectfully disagree.

The instantly claimed methods describe comparing gene expression in lung cancer cells with previously determined levels of the gene in cells with known sensitivity to agents to determine the sensitivity of cells to a drug, as described in the specification (Determination of IGEI, paragraphs [0187] to [0191]). Furthermore, the specification teaches a person of ordinary skill in the arts how gene expression data is obtained, ratios generated, statistical analysis performed, and IGEIs chosen and validated (see Examples). Thus, the specification provides guidance without undue experimentation for a person of ordinary skills in the arts to perform these methods on a cell known to be sensitive or resistant to an agent to generate IGEI values and to use those values to predict the effectiveness of an agent on other cells. Furthermore, the teachings enable one with ordinary skills in the arts to monitor treatment as the methods used as described in the specification can easily be used in monitoring any change in IGEI values. For

example, a sample may exhibit an initial IGEI value that is comparable to an IGEI value for a cell with known sensitivity to a drug, but it changes to a value that is comparable to an IGEI value for cells with known resistance.

The Examiner also asserts that because the art of determining an association between gene expression levels and a phenotype, such as responsiveness to treatment, is highly unpredictable, knowledge that gene expression levels are correlated with response to one type of therapy does not allow one to predict whether gene expression levels will be correlated with other types of therapy. Applicants respectfully disagree. The instantly claimed methods determine associations based on levels of known gene expression in cells with known responsiveness and thus would not be unpredictable. Furthermore, the specification teaches validation of the models generated (see for example, [0220]) and how IGEI are better predictors of phenotypes than are the expression levels of individual genes. The references cited by the Examiner to illustrate the unpredictability further exemplifies the innovation of the instantly claimed invention as the references do not generate a model of IGEI values and selecting validated IGEI values for use in predicting and monitoring cancer treatments.

Based on the reasons provided above, withdrawal of the rejection under 35 U.S.C. 112, first paragraph, is respectfully requested as the specification enables one of skill the art to practice the invention as it is claimed.

CONCLUSION

For the foregoing reasons, Applicants request the Examiner allow claims 1-4, 6, 7, 10-17, 19, 20, 23-30, 32, 33, 36-43, 45, 46, 49-52, 57, 82, and 90 and advance the application to issuance.

FEE AUTHORIZATION

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. **23-2415** (Docket No. 31169-705.831).

Respectfully submitted,

Date: June 11, 2009

By: _____
Angie S. Mah
Registration No. L040

WILSON SONSINI GOODRICH & ROSATI
650 Page Mill Road
Palo Alto, CA 94304-1050
Direct Dial: (202) 973-8866
Customer No. 21971